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Miliary Tuberculosis and CMV Infection in a Kidney Recipient

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Abstract

Cytomegalovirus (CMV) is the leading cause of infectious complications after organ transplantation. Tuberculosis can occur in the early postoperative period and is potentially curable. We report here a 45-year-old renal transplant recipient with a rare coinfection of CMV infection and miliary tuberculosis, as early as 6 months after the transplant. The organism was isolated from sputum and broncoalveolar lavage (BAL) specimen cultures. The patient was given 12 months of quadruple anti-TB therapy. With antituberculous therapy, and reduction in the patient's conventional immunosuppression, intravenous ganciclovir was also used. The patient remained disease-free after a follow-up period of 6 years.

To our knowledge, this is the first case report of a coinfection with cytomegalovirus and Mycobacterium tuberculosis presenting with pulmonary miliary pattern. Our patient had several risk factors such as the administration of steroid boluses and cytomegalovirus infection.

Conclusions: Post-transplant TB is a serious problem worldwide, and must be always included in the differential diagnosis of fever and pulmonary disease in the renal transplant recipient. Early diagnosis and prompt initiation of treatment for TB among renal transplant patients is very important and vital.

***Keywords*:** Cytomegalovirus, Miliary Tuberculosis, Transplantation, Renal Recipient, Coinfection

Introduction

Infection is an important problem following renal transplantation. Although advances in immunosuppressive therapy have led to increased survival of renal recipients, there are greater risks of developing infectious complications (1). Mycobacterium tuberculosis (TB) infection is still one of the life-threatening infections worldwide among renal transplants, because of their chronic immunosuppression, often with delayed diagnosis (2). All around the world TB is more common in renal allograft recipients than the general population. Its incidence is 0.5% to 1% in the United States, 1% to 4% in Europe, 3.5% in Saudi Arabia, 5.7% to 11.5% in India, 4.2% in Turkey, and 1.4% in Iran (3). Cytomegalovirus (CMV) infection is common after renal transplantation, and may predispose the patients to secondary bacterial or fungal infections. However, simultaneous coinfection is rare and often makes diagnosis difficult (4). We report a case of CMV infection in a renal transplant recipient presenting with elevated CMV pp65 antigen level and abnormal chest radiograph due to miliary tuberculosis.

Case Report

A 59-year-old woman was admitted due to general

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weakness, anorexia and fever. She had undergone living unrelated kidney transplantation 6 months previously. She was on hemodialysis due to end stage renal disease with unknown origin for 31 months. HCV Ab was positive with normal liver function tests and the tuberculin skin test was negative before kidney transplantation. Her immunosuppression was cyclosporine based. She experienced an episode of acute rejection within the first month after operation that was treated by a course of methylprednisolone pulses. One month before admission, she had intermittent fever. On admission, she complained of anorexia, nausea, weakening, cough and tachypnea. The chest radiograph revealed a miliary pattern.

Clinical work-up showed fever of 39.3°C, weight loss of 4 kg over a period of 1-2 months, cough and moderate dyspnea. Other physical examinations were unremarkable. Laboratory tests also revealed the following: serum creatinine 1.6 mg/dl, hemoglobin 10.1 g/dl, blood leucocytes 6600/mm^3, platelets 210 000/mm^3, erythrocyte sedimentation rate 45 mm/h, tuberculin (PPD) test less than 5 mm, AST 78 IU/L and ALT 34 IU/L. On hospital day 2, the patient had also been diagnosed to have CMV infection that was confirmed via a positive PP65 antigenemia assay (10 cells/100,000) and rising of the CMV IgM antibody titer (2.5 times of normal value); and therefore, ganciclovir was added to broad-spectrum antibiotics. Direct examination of sputum using by Ziehl–Neelsen-stain was performed. Transbronchial biopsy and bronchoalveolar lavage were also obtained. Histologic examination of the lesion showed non specific inflammatory process and did not reveal granuloma formation. Acid-fast bacilli were, however, present on the Ziehl–Neelsen-stained smear of respiratory specimens and Mycobacterium tuberculosis grew on the culture of sputum and bronchoalveolar lavage samples. Thus, the diagnosis of miliary tuberculosis was confirmed and the patient was treated with quadruple anti-TB therapy includes isoniazid, rifampin, pyrazinamide and ethambutol for the first 2 months, with which her clinical condition improved; followed by isoniazid and rifampin for another 10 months. Anti-TB therapy led to a complete resolution of TB lesions. In addition, CMV antigenemia became negative after 2 weeks of parenteral ganciclovir.

To our knowledge, our patient is the first case report of a coinfection with cytomegalovirus and Mycobacterium tuberculosis presenting with diffuse pulmonary miliary lesions after kidney transplantation in Iran. The patient remained disease-free after a follow-up period of 6 years.

Discussion

TB is an important infection encountered after renal transplantation, especially among patients receiving multiple immunosuppressive drugs in developing countries, where there are high incidences of morbidity and mortality (5). Reactivation of dormant infection is the usual mode of acquisition, and nosocomial transmission occurs infrequently. Donor-transmitted extra pulmonary infection has been reported. Immunosuppression assists reactivation of latent tuberculosis or progression of acquired disease in kidney transplant recipients (5).

Apaydin *et al* reported that the incidence of tuberculosis in kidney graft recipients was 5.8% (16/274) with five patients presenting with miliary tuberculosis at the time of diagnosis (6). It seems that the incidence of TB infection following renal transplantation in Iran is lower than in Saudi Arabia, India and Turkey (3). Basiri *et al* showed that among patients who had received a kidney transplant in 15 university teaching hospitals from different geographic areas in Iran between 1984 and 2003, 120 (1%) developed tuberculosis. Radiological features of Miliary pattern in Chest X-ray was observed in 9 cases (5).

The risk factors for tuberculosis in transplant patients are as yet poorly defined, although the role of intensified immunosuppression for a failing graft appears to be important. Patients who receive kidney

grafts are at an increased risk for the development of mycobacterial disease, because of uremia and the immunosuppressants used in the post-transplant period, all of which interfere with T-cell function (7). The presence of co-existing infections, such as deep mycoses, and infections due to cytomegalovirus (CMV), pneumocystis carinii or nocardia, is also closely related to the development of TB (8). In a prospective study, treatment with cyclosporine and tacrolimus was associated with an earlier onset of TB when compared with prednisolone and azathioprine (2). Immunosuppression with tacrolimus or mycophenolate mofetil is associated with the development of TB earlier in the post-transplant period and in younger patients (9). Longer history of hemodialysis enhances immunosuppression and is associated with increased probability of posttransplant TB compared with controls (5). As mentioned before, our patient presented as early as 6 months following renal transplantation and was treated with cyclosporine and prednisolone. A history of graft rejection and the use of steroid pulses, the previous long period of renal replacement therapy with hemodialysis and concomitant cytomegalovirus infection were present in our patient as potential risk factors for developing TB.

The risk of hepatotoxicity is relatively higher in patient populations such as renal recipient, with high prevalence of infection with one or both of hepatitis B and C. We saw some degree of hepatotoxicity in our patient who had hepatitis C before transplantation, and was successfully treated by reducing the dose of rifampin.

This is the first case report of a coinfection with cytomegalovirus and Mycobacterium tuberculosis presenting with diffuse pulmonary miliary lesions in Iran. Miliary tuberculosis is the most lethal form of tubercular disease. If dissemination of tubercle bacilli occurs without therapy, death is almost certain. The importance of establishing an etiologic diagnosis as promptly as possible in patients receiving immunosuppressive therapy is self-explanatory. The presence of a life-threatening infection in these patients requires aggressive antimicrobial therapy and discontinuation or decrease of the immunosuppressive drugs until the infectious process is under control.

Conflict of interest

None declared

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